

CLAIMS

1. A functional  $\alpha$  subunit of a heterotrimeric G protein comprising an amino acid sequence encoding a fluorescent or luminescent protein.
2. The protein of claim 1 wherein the amino acid sequence encoding a fluorescent or luminescent protein is cyan fluorescent protein.
3. The protein of claim 1 wherein the amino acid sequence encoding a fluorescent or luminescent protein is yellow fluorescent protein.
4. The protein of claim 1 wherein the heterotrimeric G protein is  $G\alpha 2$  of *D. discoideum*.
5. The protein of claim 1 wherein said subunit has a helical domain and said amino acid sequence is within the helical domain of said subunit.
6. A functional  $\beta$  subunit of a heterotrimeric G protein comprising an amino acid sequence encoding a fluorescent or luminescent protein.
7. The protein of claim 6 wherein the amino acid sequence encoding a fluorescent or luminescent protein is cyan fluorescent protein.
8. The protein of claim 6 wherein the amino acid sequence encoding a fluorescent or luminescent protein is yellow fluorescent protein.
9. The protein of claim 6 wherein the heterotrimeric G protein is  $G\beta$  of *D. discoideum*.
10. The protein of claim 6 wherein said amino acid sequence is at the  $\beta$  subunit's N-terminus.
11. A functional heterotrimeric G protein comprising an  $\alpha$  subunit comprising a first amino acid sequence encoding a first fluorescent or luminescent protein and a  $\beta$  or  $\gamma$  subunit comprising a second amino acid sequence encoding a second fluorescent or luminescent protein, wherein said first and second fluorescent or luminescent proteins are capable of

fluorescence resonance energy transfer (FRET) or bioluminescence resonance energy transfer (BRET).

12. The functional heterotrimeric G protein of claim 11 wherein a  $\beta$  subunit comprises the second amino acid sequence.

13. The functional heterotrimeric G protein of claim 11 wherein said first and said second amino acid sequences are within 100 angstroms of each other.

14. The functional heterotrimeric G protein of claim 11 wherein the first fluorescent or luminescent protein is cyan fluorescent protein.

15. The functional heterotrimeric G protein of claim 11 wherein the first fluorescent or luminescent protein is yellow fluorescent protein.

16. The functional heterotrimeric G protein of claim 11 wherein the second fluorescent or luminescent protein is cyan fluorescent protein.

17. The functional heterotrimeric G protein of claim 11 wherein the second fluorescent or luminescent protein is yellow fluorescent protein.

18. The functional heterotrimeric G protein of claim 11 wherein the first fluorescent or luminescent protein is cyan fluorescent protein and the second fluorescent or luminescent protein is yellow fluorescent protein.

19. The functional heterotrimeric G protein of claim 11 wherein the first fluorescent or luminescent protein is yellow fluorescent protein and the second fluorescent or luminescent protein is cyan fluorescent protein.

20. The functional heterotrimeric G protein of claim 11 wherein said first amino acid sequence is within a helical domain of said  $\alpha$  subunit.

21. The functional heterotrimeric G protein of claim 11 wherein said second amino acid sequence is at the N-terminus of said  $\beta$  subunit.

22. The functional heterotrimeric G protein of claim 11 wherein the  $\alpha$  and  $\beta$  subunits are *D. discoideum* G protein subunits.

23. The functional heterotrimeric G protein of claim 13 wherein said first amino acid sequence is within a helical domain of said  $\alpha$  subunit and said second amino acid sequence is at the N-terminus of said  $\beta$  subunit.

24. The functional heterotrimeric G protein of claim 23 wherein the first fluorescent or luminescent protein is cyan fluorescent protein and the second fluorescent or luminescent protein is yellow fluorescent protein.

25. The functional heterotrimeric G protein of claim 24 wherein the  $\alpha$  and  $\beta$  subunits are *D. discoideum* G protein subunits.

26. A nucleic acid encoding a functional  $\alpha$  subunit of a heterotrimeric G protein which comprises an amino acid sequence encoding a fluorescent or luminescent protein.

27. The nucleic acid of claim 26 wherein the amino acid sequence encoding a fluorescent or luminescent protein is cyan fluorescent protein.

28. The nucleic acid of claim 26 wherein the amino acid sequence encoding a fluorescent or luminescent protein is yellow fluorescent protein.

29. The nucleic acid of claim 26 wherein the heterotrimeric G protein is  $G\alpha 2$  of *D. discoideum*.

30. The nucleic acid of claim 26 wherein said subunit has a helical domain and the amino acid sequence is within the helical domain of said subunit.

31. A nucleic acid encoding a functional  $\beta$  subunit of a heterotrimeric G protein which comprises an amino acid sequence encoding a fluorescent or luminescent protein.

32. The nucleic acid of claim 31 wherein the amino acid sequence encoding a fluorescent or luminescent protein is cyan fluorescent protein.

33. The nucleic acid of claim 31 wherein the amino acid sequence encoding a fluorescent or luminescent protein is yellow fluorescent protein.

34. The nucleic acid of claim 31 wherein the heterotrimeric G protein is  $G\beta$  of *D. discoideum*.

35. The nucleic acid of claim 31 wherein the amino acid sequence is at the  $\beta$  subunit's N-terminus.

36. The nucleic acid of claim 26 wherein the nucleic acid comprises a vector for replication and expression of said subunit.

37. The nucleic acid of claim 31 wherein the nucleic acid comprises a vector for replication and expression of said subunit.

38. A eukaryotic cell comprising a nucleic acid according to any of claims 26 to 37

39. A eukaryotic cell which comprises: (a) a nucleic acid encoding a functional  $\alpha$  subunit or a heterotrimeric G protein which comprises an amino acid sequence encoding a first fluorescent or luminescent protein; and (b) a nucleic acid encoding a functional  $\beta$  or  $\gamma$  subunit of a heterotrimeric G protein which comprises an amino acid sequence encoding a second fluorescent or luminescent protein, wherein the cell expresses a functional heterotrimeric G protein which is capable of FRET or BRET.

40. The eukaryotic cell of claim 39 wherein the second fluorescent or luminescent protein is encoded in the  $\beta$  subunit.

41. The eukaryotic cell of claim 39 which further expresses a G protein coupled receptor.

42. The eukaryotic cell of claim 38 wherein the cell is a 3T3 cell.

43. The eukaryotic cell of claim 39 wherein the cell is a 3T3 cell.

44. The eukaryotic cell of claim 41 wherein the cell is a 3T3 cell.

45. The eukaryotic cell of claim 38 wherein the cell is a *D. discoideum* cell.

46. The eukaryotic cell of claim 39 wherein the cell is a *D. discoideum* cell.

47. The eukaryotic cell of claim 41 wherein the cell is a *D. discoideum* cell.

48. The eukaryotic cell of claim 41 wherein the receptor is for a ligand selected from the group consisting of: a chemoattractant, an odorant, a hormone, and a neurotransmitter.

49. A method for detecting conformational changes in a protein, comprising:

detecting changes in fluorescent resonance energy transfer (FRET) of an artificial protein subjected to a change in environmental conditions, wherein the artificial protein comprises at least two subunits, wherein a first subunit comprises a cyan fluorescent protein and a second subunit comprises a yellow fluorescent protein, wherein the cyan fluorescent protein and the yellow fluorescent protein are within 100 angstroms of each other, wherein a change in FRET indicates that the change in environmental conditions caused the artificial protein to change its conformation.

50. The method of claim 49 wherein the environmental conditions are changed by addition of a ligand for a protein which affects conformation of said artificial protein.

51. The method of claim 49 wherein the environmental conditions are changed by the addition of a protein which affects conformation of said artificial protein.

52. The method of claim 49 wherein FRET is monitored by exciting with blue light and observing fluorescence in the yellow range.

53. A method for detecting G protein coupled receptor signaling in the presence of a test sample, the method comprising:

contacting a cell according to claim 41 with a test sample;

monitoring fluorescence resonance energy transfer (FRET) or bioluminescence resonance energy transfer (BRET) in said cell; wherein a change in FRET or BRET suggests that the test sample binds to a G protein coupled receptor expressed in the cell.

54. The method of claim 53 wherein the cell is in a tissue sample.

55. The method of claim 53 wherein the cell is in a whole organ.

56. A functional heterotrimeric G protein comprising an  $\alpha$  subunit comprising a first fluorescent or luminescent moiety and a  $\beta$  or  $\gamma$  subunit comprising a second fluorescent or luminescent moiety, wherein the first and second fluorescent or luminescent moieties are capable of fluorescence resonance energy transfer (FRET) or bioluminescence resonance energy transfer (BRET).

57. The functional heterotrimeric G protein of claim 56 wherein a  $\beta$  subunit comprises the second fluorescent or luminescent moiety.

58. A eukaryotic cell comprising the G protein of claim 56.

59. The eukaryotic cell of claim 58 wherein said first and second fluorescent or luminescent moieties is an amino acid sequence.

60. The eukaryotic cell of claim 59 wherein one of said first and second fluorescent or luminescent moieties is luciferase.

61. A functional heterotrimeric G protein comprising an  $\alpha$  subunit comprising a fluorescent or luminescent moiety and a  $\beta$  or  $\gamma$  subunit comprising a quenching moiety, wherein the quenching moiety is capable of quenching fluorescence of the fluorescent moiety or the luminescence of the luminescent moiety.

62. A functional heterotrimeric G protein comprising an  $\alpha$  subunit comprising a quenching moiety and a  $\beta$  or  $\gamma$  subunit comprising a fluorescent or luminescent moiety, wherein the quenching moiety is capable of quenching fluorescence of the fluorescent moiety or the luminescence of the luminescent moiety.

63. The G protein of claim 61 or 62 wherein the fluorescent and quenching moieties are within 100 angstroms of each other.

64. A functional  $\gamma$  subunit of a heterotrimeric G protein comprising an amino acid sequence encoding a fluorescent or luminescent protein.

65. The protein of claim 64 wherein the fluorescent or luminescent protein is cyan fluorescent protein.

66. The protein of claim 64 wherein the fluorescent or luminescent protein is yellow fluorescent protein.

67. The protein of claim 64 wherein the heterotrimeric G protein is G $\gamma$  of *D. discoideum*.

68. The protein of claim 64 wherein said amino acid sequence is at the  $\gamma$  subunit's N-terminus.

69. The protein of claim 64 wherein the fluorescent or luminescent moiety is an amino acid sequence.

70. A nucleic acid encoding a functional  $\gamma$  subunit of a heterotrimeric G protein which comprises an amino acid sequence encoding a fluorescent or luminescent protein.

71. The nucleic acid of claim 70 wherein the fluorescent or luminescent protein is cyan fluorescent protein.

72. The nucleic acid of claim 70 wherein the fluorescent or luminescent protein is yellow fluorescent protein.

73. The nucleic acid of claim 70 wherein the heterotrimeric G protein is G $\gamma$  of *D. discoideum*.

74. The nucleic acid of claim 70 wherein the amino acid sequence is at the  $\gamma$  subunit's N-terminus.

75. The nucleic acid of claim 70 wherein the nucleic acid comprises a vector for replication and expression of said subunit.

76. A eukaryotic cell comprising a nucleic acid according to any of claims 70 to 75.